CLAIMS

1. A DNA expression cassette comprising a double-stranded randomized DNA sequence between 16-25 bases long having a first and a second end, each end operably linked to a pol III promoter having a TATA box, wherein each of the promoters is modified by substitution of:

a. at least four consecutive adenylyl residues positioned 3' to the TATA box; and,

b. from 0 to 20 bases 5' to the at least four consecutive adenylyl residues and 3' to the TATA box;

whereby transcription of the double stranded randomized DNA sequence from the promoters produces a dsRNA.

2. The DNA expression cassette of claim 1, wherein the 0 to 20 bases is at least one base and comprises a restriction site.

3. The DNA expression cassette of claim 1, wherein the promoters are the same.

4. The DNA expression cassette of claim 1, wherein the promoters are different.

5. The DNA expression cassette of claim 1, wherein the promoters are selected from the group consisting of H1 RNA promoters, U6 snRNA promoters, promoters for tRNA genes, and promoters for the adenovirus VA genes.

6. The DNA expression cassette of claim 1, wherein the randomized DNA sequence is between 17-23 bases long.

7. The DNA expression cassette of claim 1, wherein a first base transcribed in each strand of the randomized DNA sequence is G or A.

8. The DNA expression cassette of claim 1, further comprising an inducible operator sequence 5' to the TATA box.

9. The DNA expression cassette of claim 8, wherein the inducible operator sequence is the tet O operator.

10. The DNA expression cassette of claim 1, further comprising a viral particle for packaging a nucleic acid comprising the expression cassette.

11. A self-replicating DNA comprising the DNA expression cassette of claim 1.

12. A library of DNA expression cassettes, each expression cassette comprising a double-stranded randomized DNA sequence between 16-25 bases long having a first and a second end, each end operably linked to a pol III promoter having a TATA box, wherein each promoter is modified by substitution of:

a. at least four consecutive adenylyl residues positioned 3' to the TATA box; and,

b. from 0 to 20 bases 5' to the at least four consecutive adenylyl residues and 3' to the TATA box;

whereby transcription of the double stranded randomized DNA sequence from the promoters of each DNA expression cassette produces a different dsRNA.

13. The library of claim 12, wherein each of the randomized DNA sequences is between 17-23 bases long.

14. The library of claim 12, wherein the promoters are inducible.

15. The library of claim 12, wherein each DNA expression cassette is packaged in a viral particle.

16. The library of claim 12, wherein each DNA expression cassette is included in a cell genome.

17. The library of claim 12, wherein each DNA expression cassette is self-replicating.

18. A method for producing a library of DNA expression cassettes for expressing dsRNA having randomized sequences, the method comprising:

a. synthesizing a plurality of single-stranded randomized DNA sequences between 16 and 25 bases long, having a 5' and a 3' end;

b. constructing a plurality of expression vectors, each having a first and a second pol III promoter with a TATA box, wherein the first promoter is oriented to initiate transcription in the direction of the second promoter and the second promoter is oriented to initiate transcription in the direction of the first promoter, each promoter modified by substitution of:

i. at least four consecutive adenylyl residues positioned 3' to the TATA box; and,

ii. from 0 to 20 bases 5' to the at least four consecutive adenylyl residues and 3' to the TATA box;

c. inserting one of the plurality of single-stranded randomized DNA sequences between the first promoter and the second promoter of each expression vector wherein the single-stranded randomized DNA sequence is operably linked to the first promoter; and

d. generating a DNA sequence complementary to each single- stranded randomized DNA sequence, the complementary DNA sequence being operably linked to the second promoter.

19. The method of claim 18, wherein the 0 to 20 bases of the constructing step is at least one base and comprises at least one restriction site.

20. The method of claim 18, wherein the generating step further comprises transforming competent bacteria with the plurality of expression vectors comprising the single stranded randomized DNA sequences.

21. The method of claim 18, wherein the generating step comprises *in vitro* synthesis of a DNA sequence complementary to each of the plurality of single-stranded randomized nucleic acid sequence using Klenow polymerase.

22. The method of claim 18, wherein the constructing step further comprises insertion of a guanylyl residue at the 5' end of each single-stranded randomized DNA sequence and

a cytosyl residue at the 3'end, or an adenylyl residue at the 5' end of each single-stranded randomized DNA sequence and a thymidyl residue at the 3' end.

23. A method of correlating expression of a transcription sequence for an siRNA with a phenotypic change resulting from inhibiting expression of a cellular gene by the siRNA, where expression of the cellular gene is not previously characterized as contributing to the phenotypic change, the method comprising:

a. introducing to a cell population a library of exogenous randomized siRNAs, wherein each siRNA is produced from an expression cassette comprising a double-stranded randomized DNA sequence between 16-25 bases long, having a first end and second end, each end operably linked to a pol III promoter having a TATA box, wherein each promoter is modified by substitution of:

i. at least four consecutive adenylyl residues positioned 3' to the TATA box; and,

ii. from 0 to 20 bases 5' to the at least four consecutive adenylyl residues and 3' to the TATA box;

b. detecting a phenotypic difference between the cells of the population introduced to the library of siRNAs and those cells not introduced to the library; and

c. identifying the siRNA of the library responsible for the phenotypic change.

24. The method of claim 23, further comprising isolating the siRNA of the library responsible for the phenotypic change.

25. The method of claim 23, wherein the introducing step comprises transducing the cell population by means of a viral transduction system.

26. The method of claim 23, wherein the detecting step comprises observation of a difference in cellular growth between the cells of the population introduced to the library of siRNAs and those cells not introduced to the library.

27. The method of claim 23, wherein the detecting step comprises co-expression of a detectable marker by the cells of the population introduced to the library of siRNAs.

28. The method of claim 27, wherein the detectable marker is selected from the group comprising a fluorescent protein, a cell surface protein, and a drug resistance gene.

29. The method of claim 23, wherein the cell population of the introducing step is a eukaryotic cell population.

30. The method of claim 23, wherein the phenotypic difference of the detecting step comprises inhibition of cell division, or viral gene expression, or excretion of an extracellular protein, or expression of a cell surface marker, or a genetic suppressor, or a signal transduction pathway, or cell death.